

Claims:

1. A method for categorising nucleic acid, which method comprises producing a nucleic acid population by action of an endonuclease on double-stranded nucleic acid, such that each nucleic acid in the nucleic acid population has a double-stranded portion, contacting the nucleic acid population with one or more oligonucleotide sequences, and isolating nucleic acid which correctly hybridises to an oligonucleotide sequence by capturing the oligonucleotide sequence on a solid phase, wherein each oligonucleotide sequence has a pre-determined recognition sequence, the nucleic acid being categorised by its ability to correctly hybridise to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognises a sequence in the double-stranded portion of the nucleic acid, one or more different recognition sequences being represented in the oligonucleotide sequences.

2. A method according to claim 1, wherein the endonuclease is selected such that each nucleic acid in the nucleic acid population has a sticky end of a known common length extending from a terminal of its double-stranded portion.

3. A method according to claim 1, wherein the endonuclease is selected such that each sticky end of each nucleic acid in the nucleic acid population has the same known base sequence.

4. A method according to claim 3, wherein prior to contacting the nucleic acid population with the oligonucleotide sequences, the nucleic acid population is contacted with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein the adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population.

5. A method according to claim 4, wherein each oligonucleotide sequence comprises a first sequence, a second sequence attached to the first sequence and a third sequence attached to the second sequence, in which the first sequence is complementary to the sequence of the primer portion of the adaptor, the second sequence is complementary to the known sticky end

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of the nucleic acids in the nucleic acid population, and the third sequence comprises the pre-determined recognition sequence.

6. A method according to ~~claim 2~~, wherein the endonuclease is selected such that the sticky ends of the nucleic acids in the nucleic acid population have a plurality of different base sequences.

7. A method according to claim 6, wherein prior to contacting the nucleic acid population with the oligonucleotide sequences, the nucleic acid population is contacted with an array of adaptors to ligate an adaptor to a terminal of the nucleic acids in the nucleic acid population, wherein each adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion of the same length as the sticky ends of the nucleic acids in the nucleic acid population, all of the possible base sequences of the single-stranded portion of the adaptor being represented in the array of adaptors.

8. A method according to claim 7, wherein each oligonucleotide sequence comprises a first sequence, a second sequence attached to the first sequence and a third sequence attached to the second sequence, in which the first sequence is complementary to the sequence of the primer portion of the adaptors, the second sequence is of the same length as the sticky ends of the nucleic acids in the nucleic acid population, and the third sequence comprises the pre-determined recognition sequence, and wherein in any one group of oligonucleotides having the same recognition sequence all of the possible base sequences of the second sequence are represented.

9. A method according to claim 5 or claim 8, wherein the recognition sequence consists of one base.

10. A method according to claim 5 or claim 8, wherein the recognition sequence consists of two or more bases.

11. A method according to any of claims 5 and 8-10, wherein in any one group of oligonucleotides having the same recognition sequence the third sequence consists of the

recognition sequence and a pre-determined number of bases situated between the second sequence and the recognition sequence, all possible sequences of the pre-determined number of bases in the third sequence being represented in that group of oligonucleotides.

a 12. A method according to claim 1, wherein the nucleic acid population is amplified by PCR prior to reaction with the oligonucleotide sequences.

a 13. A method according to claim 1, wherein those nucleic acids are isolated both terminals of which correctly hybridise to an oligonucleotide sequence.

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14. A method according to claim 13, wherein a first set of oligonucleotide sequences is contacted with the nucleic acid population in a first step by denaturing the nucleic acid population in the presence of the first set of sequences to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first sequences, immobilising those nucleic acids which correctly hybridise to the first sequences, extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid, denaturing the double-stranded nucleic acid and removing non-immobilised species to isolate the resulting immobilised single-stranded nucleic acid, contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences in a second step, extending the correctly hybridised oligonucleotide sequences along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid, denaturing the double-stranded nucleic acid and isolating the resulting non-immobilised single-stranded nucleic acid.

15. A method according to claim 14, wherein the extended and isolated products of the first step and/or the extended and isolated products of the second step are amplified by PCR.

a 16. A method according to claim 14 or claim 15, wherein the correctly hybridised nucleic acids are immobilised by immobilising the oligonucleotide sequences.

17. A method according to claim 16, wherein each oligonucleotide in the first set of sequences carries a biotin residue such that prior to or after hybridising to the nucleic acid the sequence is captured on an avidinated solid phase.

18. A method according to claim 16, wherein each oligonucleotide in the first set of sequences is covalently attached to a solid support prior to contacting with the nucleic acid population.

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19. A method according to *claim 14* ~~any of claims 14-18~~, wherein the recognition sequence of the first and second set of oligonucleotide sequences consists of one base and, prior to performing the first step, the nucleic acid population is sub-divided into 16 wells, each well containing oligonucleotides from the first set of sequences having one of the four possible recognition sequences, and wherein in the second step oligonucleotides from the second set of sequences are added to each well, such that all possible combinations of the identities of the first and second set of oligonucleotide sequences and their order of addition to the well are represented in the 16 wells.

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20. A method according to *claim 14* ~~any of claims 14-18~~, wherein the recognition sequence of the first and second set of oligonucleotide sequences consists of two bases and, prior to performing the first step, the nucleic acid population is sub-divided into 256 wells, each well containing oligonucleotides from the first set of sequences having one of the 16 possible recognition sequences, and wherein in the second reaction oligonucleotides from the second set of sequences are added to each well, such that all possible combinations of the identity of the first and second set of oligonucleotide sequences and their order of addition to the well are represented in the 256 wells.

21. A method according to claim 19, wherein the contents of each pair of wells to which the same pair of oligonucleotide sequences were added but in a different order, are combined to give 10 different wells.

22. A method according to claim 20, wherein the contents of each pair of wells to which the same pair of oligonucleotide sequences were added but in a different order, are combined to give 136 different wells.

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a ~~23. A method according to any preceding claim, wherein the oligonucleotide sequences have equalised melting temperatures.~~

24. A method according to claim 23, wherein the melting temperatures are equalised by incorporating one or more analogues of natural nucleotides into the oligonucleotide sequences, the analogues comprising base modifications, sugar modifications and/or backbone modifications.

a ~~25. A method according to any preceding claim, wherein the endonuclease is selected such that it cuts the nucleic acid at a site within the recognition site of the endonuclease.~~

26. A kit for categorising a nucleic acid, comprising one or more adaptors and one or more sets of oligonucleotide sequences, wherein the adaptors comprise nucleic acid having a double-stranded primer portion of a known sequence and a single-stranded portion of a pre-determined length, either each single-stranded portion of each nucleic acid in the adaptors having the same pre-determined sequence or all possible sequences of the single-stranded portion being represented in the adaptors, and wherein each oligonucleotide sequence comprises a first sequence, a second sequence attached to the first sequence and a third sequence attached to the second sequence, in which the first sequence is complementary to the sequence of the primer portion of the adaptor, the second sequence is the same sequence as the single-stranded portion of the adaptors or all possible second sequences of the same length as the single-stranded portion of the adaptors are represented within the set of oligonucleotides, and the third sequence comprises a pre-determined recognition sequence.

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~~28. A kit according to claim 26, wherein in the recognition sequence consists of two or more bases.~~

a ~~29. A kit according to any of claims 26-28, wherein in any one group of oligonucleotides having the same recognition sequence, the third sequence consists of the recognition sequence and a pre-~~

determined number of bases situated between the second sequence and the recognition sequence, all of the possible sequences of the pre-determined number of bases in the third sequence being represented in that group of oligonucleotides.

a 30. A kit according to *claim 26* ~~any of claims 26-29~~, comprising two sets of oligonucleotide sequences, each of the oligonucleotides in one set being biotinylated.

a 31. A kit according to *claim 26* ~~any of claims 26-29~~, comprising two sets of oligonucleotide sequences, each of the oligonucleotides in one set being covalently attached to a solid support.

a 32. A kit according to *claim 26* ~~any of claims 26-31~~, additionally comprising an endonuclease.

33. A kit according to claim 32, wherein the endonuclease is selected such that when it is reacted with double-stranded nucleic acid, nucleic acids are produced each of which comprises a double-stranded portion.

34. A kit according to claim 33, wherein the endonuclease is selected such that the nucleic acids produced have a sticky end of a known common length extending from a terminal of the double-stranded portion, and wherein each sticky end of each nucleic acid in the nucleic acid population has the same known base sequence.

35. A kit according to claim 33, wherein the endonuclease is selected such that the nucleic acids produced have a sticky end of a known common length extending from a terminal of the double-stranded portion, and wherein the sticky ends of the nucleic acids in the nucleic acid population exhibit a plurality of different base sequences.

a 36. A kit according to *claim 26* ~~any of claims 26-35~~, wherein the endonuclease is selected such that it cuts the nucleic acid at a site within the recognition site of the endonuclease.

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